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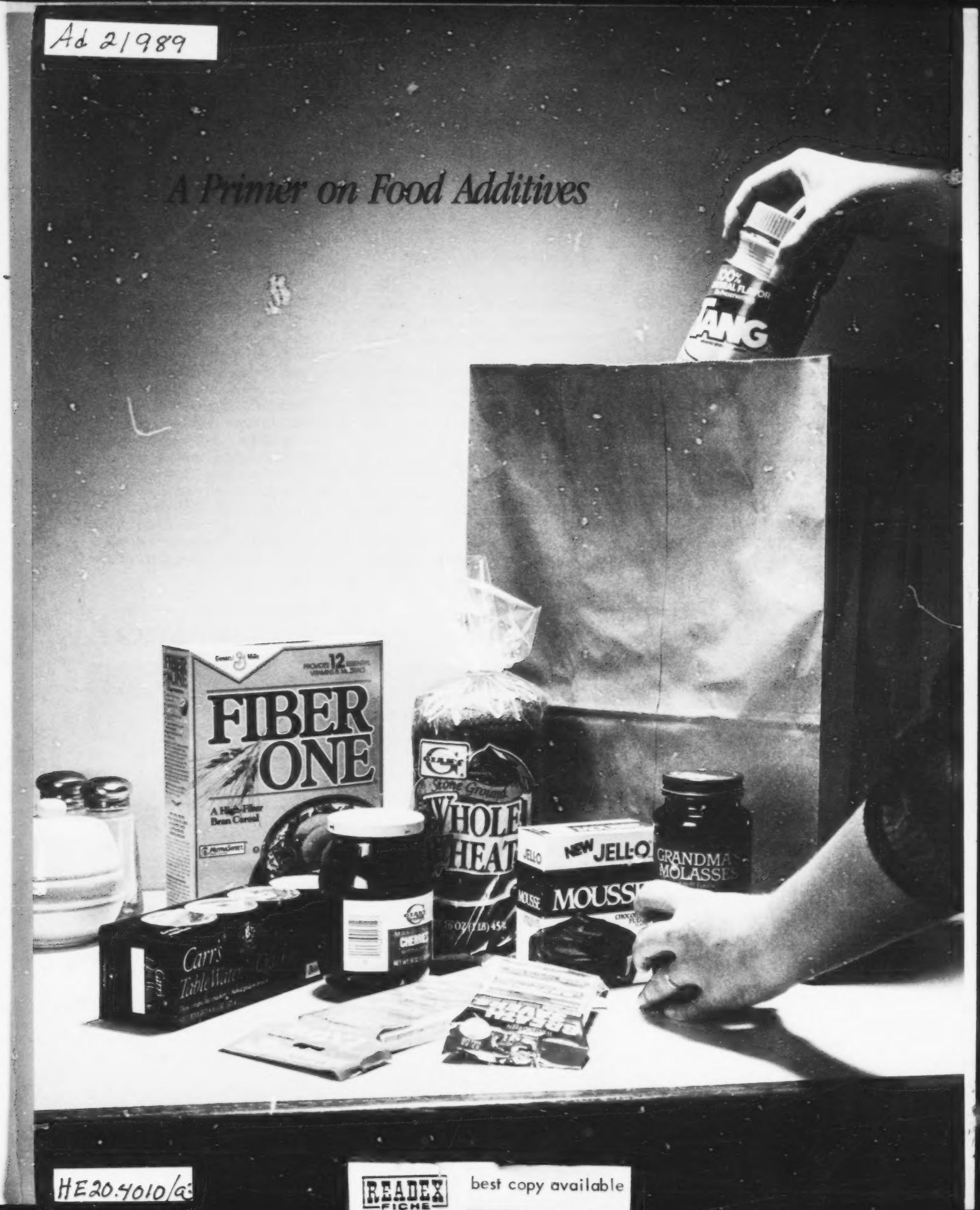

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Since the time when the kitchen stove was a campfire outside a cave, people have tinkered with ways to preserve and enhance food. Food was fragile, delicate, prone to rot, and easily injured. Bugs infested it, bacteria invaded it, mold infected it, and the air made it rancid.

Something had to be added to protect food and perhaps make it tastier, too. So the ancient Romans used sulfites to disinfect wine containers and help preserve the wine. Europeans in the 13th and 14th centuries embraced Marco Polo because he brought back spices from the Orient to season their bland diet. Travelers to the New World stored meat in salt to preserve it during their long voyages across the Atlantic Ocean. Later, pioneers in America used saltpeter to preserve their meat.

"Without food additives, we'd live like the caveman," says Richard Ronk, acting director of FDA's Center for Food Safety and Applied Nutrition.

Additives prolong the life of food, keep it from spoiling, add flavor, and help prevent disease. Without food additives bread would easily mold, cake wouldn't rise, salt would lump, ice cream would separate into icy crystals, and marshmallows would harden into bite-sized rocks.

Former generations could add just about anything they wanted to food—as long as it didn't poison someone. But increasing knowledge about food science and the possible long-term harmful effects of food chemicals on health led Congress in 1958 to enact the Food Additives Amendment to the Federal Food, Drug, and Cosmetic Act to ensure the safety of additives. In 1960 the Color Additive Amendments were enacted to make sure colorings used in foods (drugs, medical devices, and cosmetics, as well) were safe.

For purposes of FDA regulations, chemicals added to foods—other than pesticides and animal drugs—fall into four categories:

Aspartame

The artificial sweetener aspartame (brand name NutraSweet) is one of the most widely used food additives. Most people know that it's used to sweeten diet sodas, but it is also found in breakfast cereals, candy and gum—such as the products pictured here—and a wide array of other foods, as well.

Salt

Salt is an ingredient added to many foods, such as those shown here. It falls into the category of "GRAS" food additives—generally recognized as safe. Additives in this category, which includes such other common ingredients as sugar and many herbs and spices, are considered safe based on either a history of safe use before the Food Additives Amendment was passed in 1958, or the results of scientific studies.

Nitrites

Nitrites—preservatives added to many types of processed meats, including those shown here—are known as "prior sanctioned" food additives because they were approved before the 1958 Food Additives Amendment became law.

Artificial Dyes

Many of the rich, appealing colors we take for granted in today's processed foods, such as those shown here, are due to the use of color additives. According to the Color Additive Amendments of 1960, such food dyes must be safe.

- food additives,
- generally recognized as safe (GRAS) substances,
- prior-sanctioned substances, and
- color additives.

These finely drawn legal categories were set up to ensure appropriate safety reviews of food additives. Depending on what category an ingredient falls in, different regulatory requirements apply.

The "toughest" category—in terms of regulations and safety testing—is the food additive category. This covers substances that have no proven track record of safety; scientists just don't know that much about them. Additives such as the artificial sweetener aspartame and the emulsifying agent polysorbate 60, which is found in salad dressing and other food, were substances that needed to be tested before they could be used because it was not known whether they were safe. Subsequent testing proved them safe.

But what is "safe?"

"Congress has defined safety as a reasonable certainty that no harm will result from use of an additive," says Gerad McCowin, director of FDA's division of food and color additives. "In our evaluation we examine to see whether the additive has any toxic effects, whether it may cause birth defects. Does it interfere with nutrition? Does it affect individuals with allergies?"

When an additive is tested, it is usually fed in large doses over an extended period to at least two kinds of animals. These feeding studies, usually done by or for a food company that wants to use or sell the additive, are designed to determine whether the substance causes cancer, birth defects, or other injury to the animals.

Cancer is of particular concern. A special provision of the 1958 and 1960 additive amendments, the so-called Delaney clause, states that if an additive is found to cause cancer in humans or animals it may not be added to food.

The company submits the results of all these tests to FDA for review. If the FDA review finds that the additive is safe, the agency establishes regulations for how it can be used in food. This commonly includes a 100-fold margin of safety. This means that the substance may be used in food at a level that is no more than 1/100th of the highest level at which it was fed to test animals and did not produce any harmful effects.

The second group of substances is known as GRAS, an acronym for substances "generally recognized as safe." This group includes several hundred substances whose use in food experts consider safe based either on a history of safe use before 1958 or on published scientific evidence.

Congress established the GRAS category in 1958 because it felt that it was unnecessary to require industry to develop evidence to prove the safety of substances that were already generally regarded as safe by knowledgeable scientists. Included are many spices and herbs, salt, sugar, and vitamins that "logic and commonsense," in the words of one expert, tell us are safe to use.

"These are substances that are so widely known and the information about them is so widely distributed in the scientific community, that there is little question about their safety," says Dr. George Pauli, a consumer safety officer with FDA's division of food and color additives.

The third category—"prior-sanctioned" substances—include ingredients such as the preservative nitrite (used in meat) that had been sanctioned before the 1958 amendment by either FDA or the U.S. Department of Agriculture to be used in a specific food. For example, while nitrites can be used in meat, they cannot be used on vegetables because vegetables were not covered by the pre-1958 sanction.

Inclusion in either of the latter two categories—GRAS and prior sanctioned—does not guarantee a substance's safety; sometimes new evidence shows that "logic and commonsense" erred. If new data suggested that a GRAS or prior-sanctioned substance may be unsafe, then FDA requires the manufacturer to conduct studies to ascertain the ingredient's safety.

For example, the artificial sweeteners saccharin and cyclamates are substances that were once included on the GRAS list but came under fire several years ago because of new evidence that they may cause cancer in animals. Based on this evidence they were removed from the GRAS list; in fact, cyclamates were banned from use in food altogether. (Saccharin continues to be used because Congress granted it a special exemption.)

The Color Additive Amendments subject substances in the fourth category—dyes used in foods, drugs, cosmetics and medical devices—to pre-market testing similar to that required for the first category—food additives. Colors in use when the amendments were passed were placed on a provisional approval list pending further investigation to confirm their safety. Nearly 200 colors were on the provisional approval list in 1960. Since the passage of the amendment, several of the colors have been dropped because manufacturers were no longer interested in marketing them or because they were found to be unsafe.

Food additives may also be present in food packages. Known as indirect additives, they can end up in the food so FDA requires that they be evaluated.

The ubiquitous presence of additives in nearly all our foods adds up to big business. The food additive industry generates approximately $10 billion a year in business, according to Dr. Richard Hall, a former vice president with McCormick Spices.

But it is the safety of food additives that remains a key concern for FDA. The agency must be sure that the new sweeteners, emulsifiers, preservatives, dyes and other substances that food chemists concoct to add to our modern-day diet measure up to safety standards appropriate to the 1980s, not the Stone Age. ■

Reporting Reactions to Additives

by Judy Folkenberg

Some bodies just don't like certain foods. And when that happens, the body's reactions can range from headaches or hives to seizures or death.

Food additives have not been exempt from blame either. With the introduction of the artificial sweetener aspartame in soft drinks in 1983, complaints blaming food additives for allergic reactions soared. To better monitor the effects of additives and deal with consumer complaints, FDA set up the Adverse Reaction Monitoring System (ARMS) in early 1985.

The surveillance system is passive; that means FDA doesn't go out looking for adverse reactions, but investigates complaints it receives from individuals who suffer reactions or from their physicians. The NutraSweet Company—manufacturer of aspartame—also forwards complaints it receives to FDA.

FDA officials investigate the complaints, which are then classified by the severity of the symptom (headaches, mood changes, nausea, etc.) and by the frequency and consistency of the symptom's association with eating or drinking a particular product (whether the symptom occurred more than once, and how soon it occurred after the suspect product was eaten).

ARMS has received nearly 6,000 complaints since its inception. Aspartame and sulfite preservatives top the list, accounting for almost 95 percent of all complaints. Other culprits include the flavor enhancer monosodium glutamate, nitrite preservatives, the emulsifier polysorbate, and some dyes.

Even vitamin and mineral supplements have come in for their share of suspicion. There have been two reports of chemically induced hepatitis, one blamed on consumption of large quantities of a multivitamin preparation, the other on a niacin supplement.

Aspartame complainers most often blamed diet soft drinks for their symptoms. Their most frequent complaint is headaches.

Reported reactions due to sulfites have been far more serious. About 1 percent of the population is sensitive to sulfites. (Most of these individuals suffer from asthma.) Approximately 50 percent of the reported sulfite reactions were classified as serious (for example, difficulty breathing or seizures). Twenty-seven individuals (nearly all were asthmatic) may have died from sulfites, according to ARMS data.

Sulfite complainers most often traced their adverse reactions to salad bars. Since August 1986, when FDA prohibited the use of sulfites on raw fruits and vegetables—including those in salad bars—complaints about sulfites have declined. More recently, FDA has proposed keeping sulfites out of many types of potatoes served in restaurants. (For more on sulfite reactions and regulations, see "An Order of Fries—Hold the Sulfites," in the March 1988 *FDA Consumer.*)

Pinpointing a specific ingredient as the cause of an allergic reaction can be a lengthy trial-and-error process. Discovery of the exact cause has often baffled physicians and FDA.

For example, in some of the aspartame cases individuals blamed the artificial sweetener for a reaction days after they had eaten or drunk a product containing the sweetener. Was aspartame really to blame? Did all the highly publicized controversy surrounding the inclusion of aspartame in soft drinks prompt some individuals to blame health problems on aspartame? Did some individuals blame aspartame when, in fact, their adverse reactions resulted from an underlying medical disorder?

"We have no firm evidence that aspartame actually causes the number of adverse reactions that individuals claim it does," says Dr. Walter Glinsmann, associate director for clinical nutrition at FDA.

In a *New England Journal of Medicine* article on aspartame and headaches, scientists reported the results of a double-blind, placebo-controlled, cross-over study. They found that the placebo caused more headaches than aspartame.

Glinsmann notes that the number of adverse reactions individuals blame on aspartame are so varied that it is virtually impossible for one product to be guilty of such a multitude of sins. There is also no consistent relationship between a symptom and the amount of aspartame ingested or the period of time between taking aspartame and the appearance of the symptom.

"On the other hand, there is limited evidence from challenge tests [tests in which suspected allergens are given in sufficient doses to try and provoke reactions in individuals] that at least some individuals may have an allergic-type reaction such as hives to aspartame," says Glinsmann.

Three studies may help answer some of the questions surrounding aspartame and adverse reactions. The National Institute of Environmental Health Sciences in Research Triangle Park, N.C., is studying the relationship between aspartame and seizures in animals. Battelle Institute, whose headquarters is in Columbus, Ohio, is assessing the effect of aspartame on brain chemicals. And the Federal Aviation Agency will conduct a series of tests with pilots during flight-simulated computer exercises to see if aspartame affects cognition and perception.

If you suspect you have had an allergic reaction to an additive, contact your local physician for treatment. You or your doctor might want to then contact the nearest FDA field office (look in the blue pages of your phone book) to report the reaction.

For more on food allergies, see "Food Allergies: Separating Fact from 'Hype' " in the June 1986 *FDA Consumer.* ■

Judy Folkenberg is a member of FDA's public affairs staff.

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